REMARKS

Summary of the Telephonic Interview

Applicants wish to thank the Examiner for his helpful comments during the telephonic interview of February 7, 2007. Participating in the call were Paul T. Clark, Todd Armstrong, Dr. Vassilis I. Zannis, and Dr. Kyriakos E. Kypreos. The 35 U.S.C. § 112, first paragraph, rejection of pending claims 30, 34, 36, 43, 44, 47, 51, 53, 56, 58, 60-62, 72, and 79-89 was discussed.

During the interview, Applicants discussed the inventors' discovery that apoE polypeptides that include at least amino acids 1-185 of SEQ ID NO: 2 but that lack amino acids 260-299 of SEQ ID NO: 2 are capable of lowering cholesterol in a mammal without raising triglyceride levels. In addition, Applicants stated that the specification clearly discloses that apoE polypeptides further containing one or more of the additional residues between 186-259 of SEQ ID NO: 2 exhibit the same biological effect of lowering cholesterol without raising triglyceride levels. Applicants also indicated that apoE polypeptides having at least 90% sequence identity to the apoE sequence recited in the pending claims was fully described and enabled by the present specification. Finally, Applicants directed the Examiner's attention to the inventors' previously submitted data which demonstrate the successful gene therapy applications of the invention (i.e., the data show that the administration of an adenoviral vector encoding the recited apoE polypeptides lowers cholesterol without raising triglyceride levels; see Declaration of Dr. Vassilis I. Zannis, M.D. dated February 21, 2006).

Applicants indicated that they would submit an amendment to the claims that would more clearly recite the invention of present claims 30, 34, 36, 43, 44, 47, 51, 53, 56, 58, 60-62, 72, and 79-89. The Examiner agreed that he would consider amended claims which were narrowed to

recite nucleic acid molecules that encode secreted polypeptides having an amino acid sequence that includes at least amino acid residues 1-185 of SEQ ID NO:2 but that does not include the C-terminal amino acids 260-299 of SEQ ID NO:2; the claims would also cover nucleic acid molecules that encode the additional amino acid residues between 186-259 of SEQ ID NO:2. The Examiner requested that Applicants explain how the proposed amendment overcomes the previous written description and enablement rejections.

In addition, the Examiner mentioned U.S. Patent No. 5,811,243 (Strittmatter et al.) during the interview, stating that it may be relevant to the pending claims. The Examiner requested that Applicants include remarks with the supplemental claim amendment that distinguish the amended claims over this reference.

Support for the Present Amendment

By the present amendment, Applicants cancel claims 30, 34, 36, 43, 44, 47, 51, 53, 56, 58, 60-62, 72, and 80-82, amend claims 79 and 83-89, and add new claims 90-101. Support for the amendment to claims 79 and 83-89 and for new claims 90 and 96-101 is found in the specification at, e.g., page 8, lines 1-22, and page 10, lines 4-7. Support for new claims 91-95 is found in prior claims 34, 36, 43, 44, and 47. No new matter is added by the amendment.

Applicants also note the Examiner's remarks on page 3 of the Interview Summary in which the Examiner states:

> Applicants proposed to amend narrower claims that encompass the use of recombinant adenoviral vectors encoding secreted polypeptides having at least amino acid residues 1-185 of **SEQ ID NO:15 (elected species)** and those containing additional amino acid residues 186-259 of **SEQ ID NO:15**. (Interview Summary p. 3; emphasis added.)

Applicants wish to point out that SEQ ID NO:15 provides the apoE3 preprotein sequence (i.e., an apoE3 sequence that includes the 13 amino acid leader sequence as amino acids 1-13), while SEQ ID NO:2, which is recited in present claims 79 and 83-101, provides the mature apoE3 protein that lacks this leader sequence. SEQ ID NOs:2 and 15 are the same except that SEQ ID NO: 2 lacks the 13 amino acid leader sequence present in SEQ ID NO:15. Because Applicants' specification describes the apoE polypeptides relative to the mature apoE sequence (in this case apoE3, which is recited in SEQ ID NO:2), Applicants have chosen to include a reference in present claims 79 and 83-101 to SEQ ID NO:2 rather than the elected sequence of SEQ ID NO:15 to avoid confusion. Applicants further point out that present claims 96-101 are directed to apoE polypeptides that include the 13 amino acid signal sequence recited in SEQ ID NO:15.

Discussion of the Present Amendment

Applicants have amended present claims 79 and 83-101 to recite nucleic acid molecules that encode apoE polypeptides having a sequence with at least 90% sequence identity to at least amino acids 1-185 of SEQ ID NO:2 (i.e., the nucleic acid molecules that encode the apoE polypeptides can further encode the amino acid residues between amino acids 186-259 of SEQ ID NO:2), but lacking amino acids 260-299 of SEQ ID NO:2 (i.e., the residues of apoE which were identified by Applicants as responsible for causing hypertriglyceridemia in mammals). As was discussed in the Reply to Office Action filed on December 12, 2006, Applicants have demonstrated possession of the apoE polypeptides recited in present claims 79 and 83-101 based on Applicants' description of the apoE polypeptides in the present specification and the

declaratory evidence presented by Applicants on February 21, 2006, which provide several examples in which the invention of present claims 79 and 83-101 was reduced to practice. Applicants submit that one skilled in the art would recognize Applicants' possession of the invention of present claims 79 and 83-101 based on Applicants' teachings in the present specification. For this reason, Applicants have satisfied the written description requirement of 35 U.S.C. § 112, first paragraph (see M.P.E.P. § 2163).

Applicants have also demonstrated enablement of the invention of present claims 79 and 83-101. Present claims 79 and 83-101 recite both structural and functional limitations for the apoE polypeptides, which establish the metes and bounds of the recited method, and, given the breadth of Applicants' disclosure, the amount of guidance provided in Applicants' specification, the presence of working examples, and the level of skill in the art, the identification of desirable apoE polypeptides requires no more than routine methods and does not constitute undue experimentation. Thus, present claims 79 and 83-101 are enabled, even if some screening would be necessary to identify the particular apoE polypeptides needed to give the desired cholesterol-lowering effect without inducing hypertriglyceridemia. Applicants submit that the scope of present claims 79 and 83-101 is commensurate with the instant specification's scope of enablement.

For the reasons discussed above and as further elaborated in the prior Reply to Office Action dated December 12, 2006, Applicants respectfully request that the rejection of prior claims 30, 34, 36, 43, 44, 47, 51, 53, 56, 58, 60-62, 72, and 79-89 under 35 U.S.C. § 112, first paragraph, for lack of written description and enablement be withdrawn, and that this rejection not be applied to present claims 79 and 83-101.

Strittmater et al.

During the telephonic interview of February 7, 2007, the Examiner identified U.S. Patent No. 5,811,243 (Strittmatter et al.), and requested that Applicants distinguish any proposed amended claims over this reference. In response, Applicants note that present independent claims 79 and 83 have been amended to recite "a method of lowering cholesterol in a mammal in need thereof" (Emphasis added). This amendment is made to distinguish present claims 79 and 83-101 over Strittmatter, which only discloses the treatment of Alzheimer's disease by administering a viral vector that encodes apoE or a fragment thereof; Strittmatter does not disclose the treatment of mammals that require a reduction in their cholesterol levels. Thus, Strittmatter fails to teach or suggest all of the limitations of present claims 79 and 83-101. For this reason, present claims 79 and 83-101 are novel and non-obvious over Strittmatter.

CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is respectfully requested. In addition, Applicants note that the present Supplemental Amendment, which is being submitted on March 12, 2007, in response to the Interview Summary mailed on February 9, 2007, is timely filed because the deadline of March 11, 2007, for submitting a written reply to the Interview Summary (i.e., 30 days from the mailing date of the Interview Summary), falls on a Sunday.

If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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Date: 12 March 2007

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